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February 1, 2007

BY HAND DELIVERY

Sousan S. Altaie, Ph.D., Scientific Policy Advisor
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Device Evaluation and Radiological Health
Food and Drug Administration, HFZ-440
2098 Gaither Road
Rockville, MD 20850

Re: Public Meeting on the Guidance Document for IVDMIAs
Client-Matter No. 10500666

Dear Dr. Altaie:

Enclosed please find the anticipated testimony of Dr. Arthur Beaudet, Chairman of the Department of Genetics at Baylor College of Medicine, to be presented at the upcoming Public Meeting on the Guidance Document for IVDMIAs being held on February 8, 2007. We are enclosing, for your convenience, a hard copy as well as a disk of his presentation.

Yours very truly,

R. Joel Slomoff
Special Consultant

Enclosures

cc (by hand):
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 106
Rockville, MD 20852

Document Mail Center
FDA - CDRH
9200 Corporate Drive
Rockville, MD 20850

RJS//pd

20182517.1/10500666

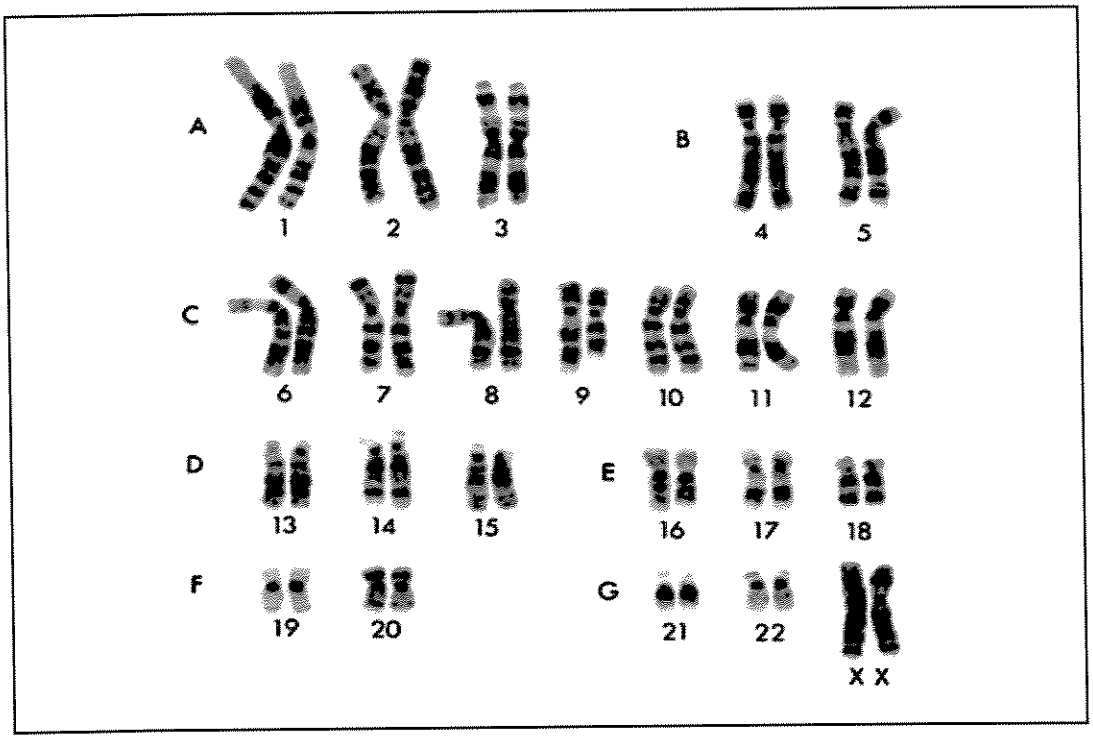
BCM
Baylor College of Medicine

Public Meeting on the Guidance Document for IVDMIAs

February 8, 2007

Arthur L. Beaudet, M.D.
abeaudet@bcm.tmc.edu
James R. Lupski, M.D.
jlupski@bcm.tmc.edu

Points to Consider on Proposed Guidance for IVDMIAs


A
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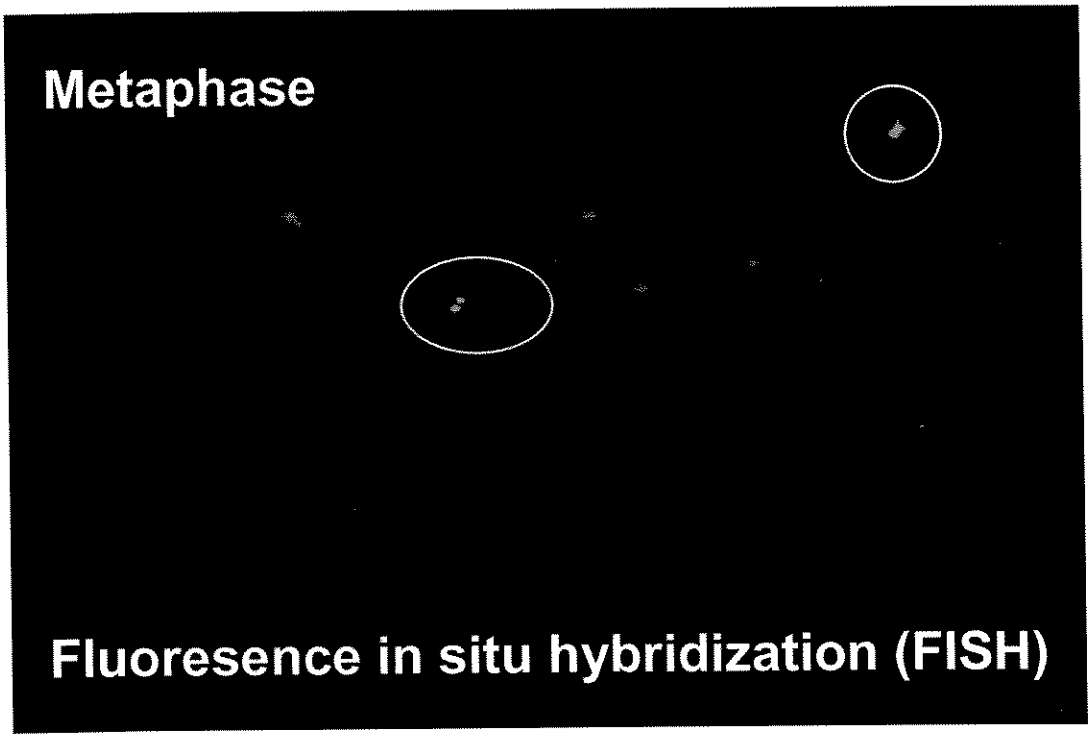
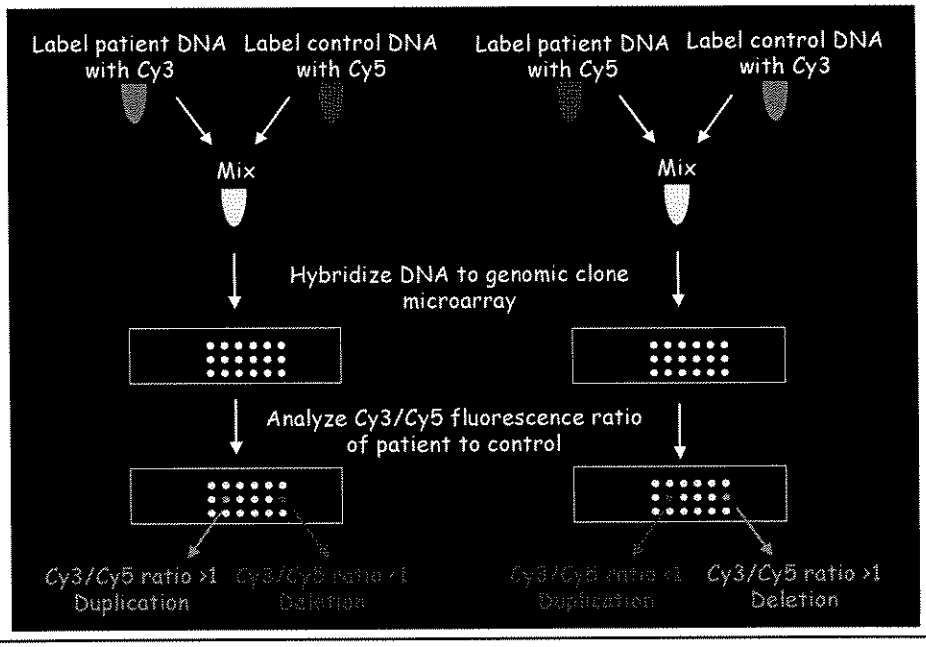

Metaphase
Fluoresence in situ hybridization (FISH)

Interphase FISH duplication

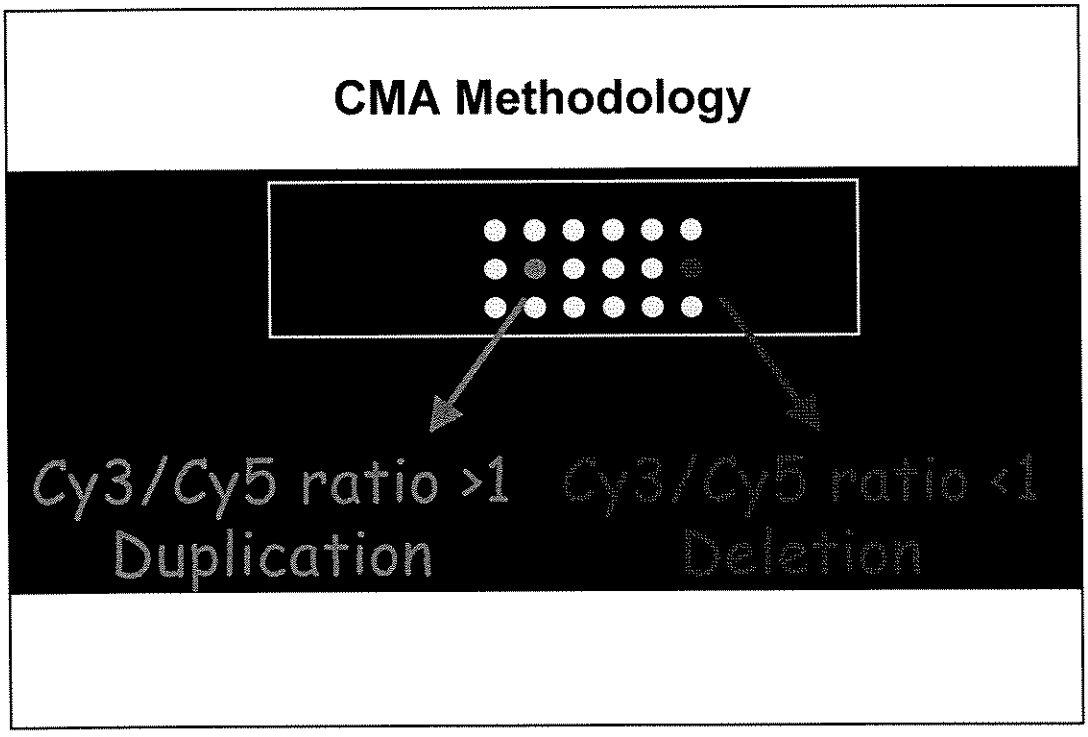
Array Comparative Genomic Hybridization (Array CGH)

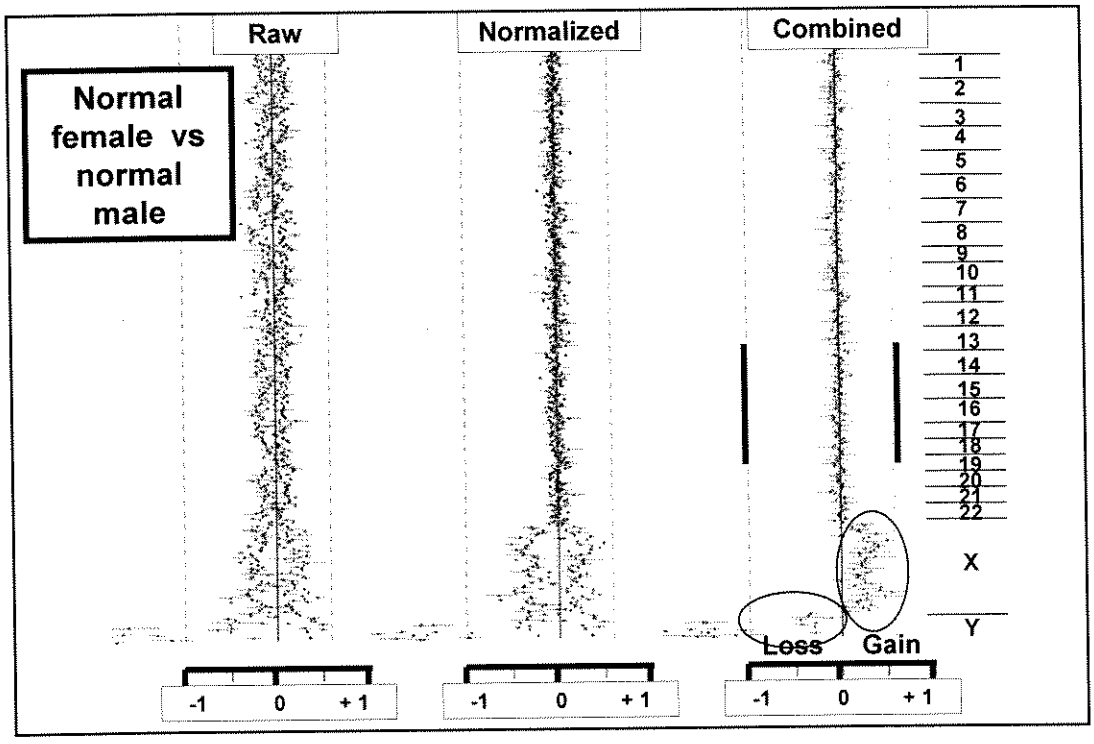
Chromosomal Microarray Analysis (CMA)

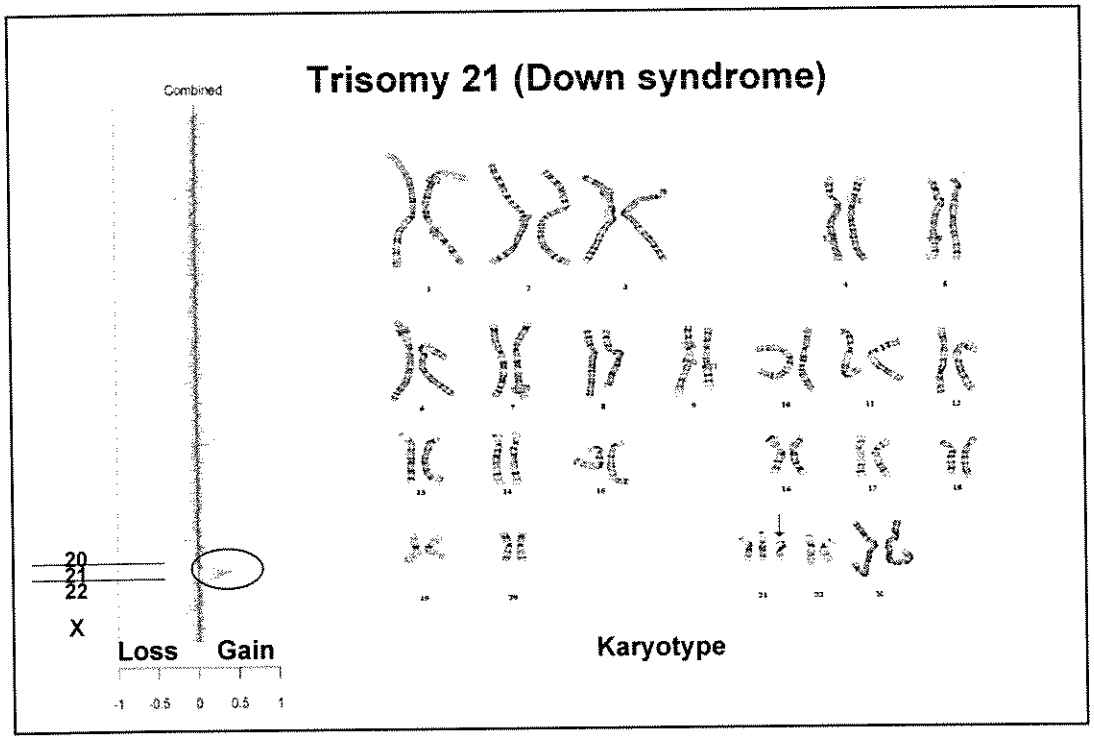
CMA Methodology



CMA Methodology

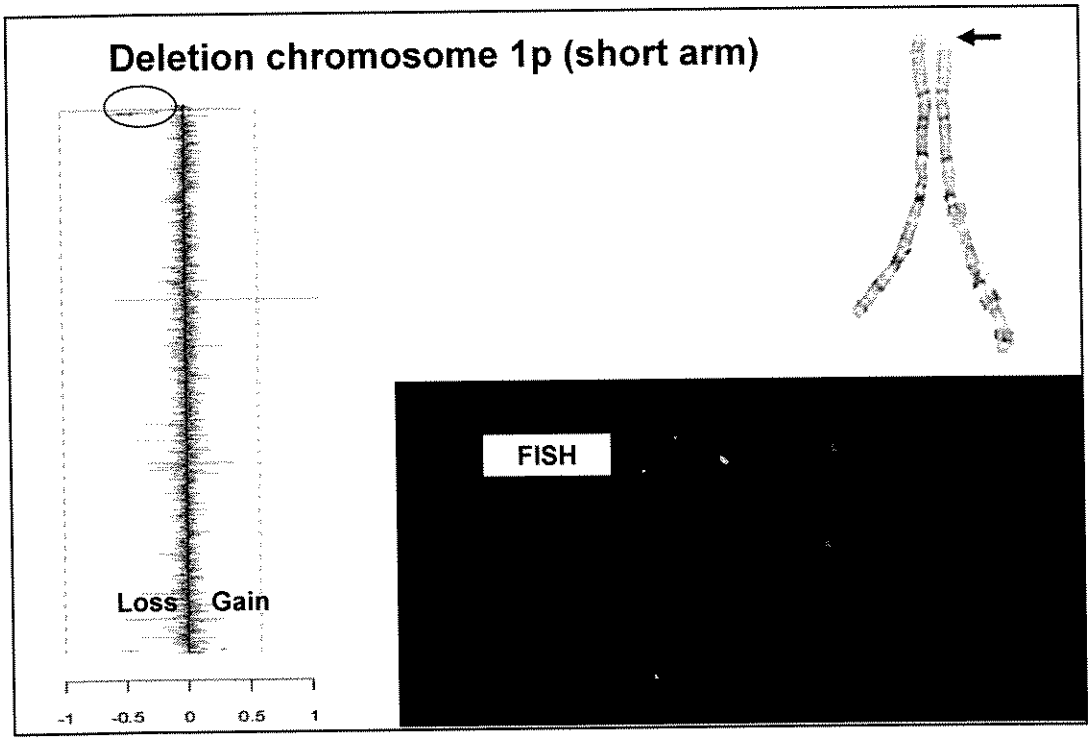



Raw
Normalized
Combined
Normal female vs normal male
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Y
Loss
Gain
-1
0
+ 1
-1
0
+ 1
-1
0
+ 1


Trisomy 21 (Down syndrome)
Combined
20
21
22
X
Loss
Gain
-1
-0.5
0
0.5
1
Karyotype

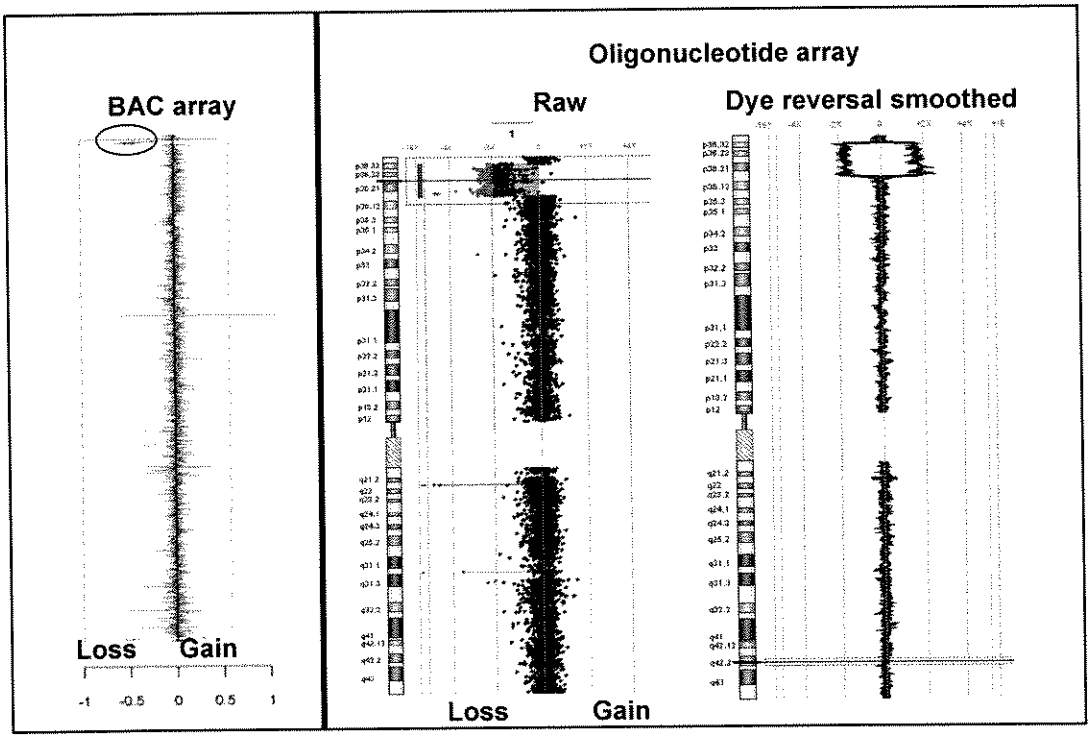
Case 2: Previous result : 46,XX (at birth)

- At two months of age
- Facial dysmorphism
- Bilateral cleft lip and palate
- Growth parameters <5th percentile
- Congenital heart disease
  - AV canal type VSD and a small ASD



PLATFORM EQUIVALENCY

- Many different platforms can provide equivalent data regarding gain or loss of copy number (BAC, oligonucleotide, or bead arrays).
- Results can be specified for genomic segments tested using nucleotide designations for human genome.



Array CGH Advantages

- Detects many abnormalities missed by karyotype.
  - –Many absolutely undetectable
  - –High variability in karyotype quality.
- Equivalent to hundreds or thousands of FISH tests at low cost.
- Particularly good for duplications.

Suggested array CGH Guidance

- Analogy to imaging devices (e.g., MRI of brain or mammography); all platforms equivalent.
- Four components
  - – Raw image data.
  - – Algorithm to process data.
  - – Interpretation by board certified laboratorian for result; regions with gain or loss and associated possible phenotypes (like radiologist).
  - – Clinician integrates result in clinical context.

Array CGH as a general test of genome copy number

- We believe that array CGH is the biggest advance in genetic diagnosis in decades.
- We believe that array CGH should replace karyotype as the primary cytogenetic test.
- Delay is depriving families of valuable diagnostic and counseling information.
- Array CGH can be less costly than karyotype.
- Array CGH is applicable to prenatal diagnosis.

END

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